

REMARKS

Applicants have canceled claims 1-5, 23-24, and 26-46 from consideration and without prejudice. Pending claims 6-22 and 25 have not been amended in this Amendment. No new matter has been added.

1. Claims 6-22 and 25 are rejected under 35 U.S.C. 103(a) as being unpatentable over Desiderio (J Chromatography B 1999;731:3-21).

The Examiner states, "Desiderio teaches a method for determining the presence/quantity of a target polypeptide in a mixture of different polypeptides by providing a mixture of human tissue extracts (from human with metabolic defects and normal control-page 5, 2.1 and 2.2), adding two known quantity of labeled (labeled differently with stable isotopes) peptide internal standard (page 5, 2.4), treating the mixture with a protease (trypsin-page 7, 2.6), fragmenting the peptides in the mixture by multistage mass spectrometry (tandem mass spectrometer-page 7, 2.8), determining the ratio of labeled fragments to unlabeled fragments and calculating the quantity of the target polypeptide in the mixture (page 7, 2.10.1 and page 8, 2.10.2).

Peptides are separated by HPLC chromatograph (page 6, under Chromatograph, 2.5.1-2.5.4) and the fractions (elutent and co-elutent) are shown in Fig. 5-7. The presence/quantity of target polypeptide is diagnostic of a cell state where the cell state is representative of an abnormal physiological response (human pituitary macroadenomas-page 9, 3.1), and the target polypeptide is determined in at least two mixtures (abstract and for details see pages 9-14, pages 14-17).

Desiderio does not teach a single peptide internal standard in the method.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to modify the method of Desiderio by using a single peptide internal standard in the method because using a single peptide internal standard is an obvious improvement over using two peptide internal standard as taught by Desiderio (page 5, 2.4). One would have been motivated to make the modification because Desiderio et al. specifically described a method for determining the presence/quantity of a target polypeptide in a mixture of different polypeptides with two peptide internal standard, and would reasonably have expected success because the two peptide internal standards taught by Desiderio displayed similar chemical, biochemical and physical behavior even though they are labeled differently (page 5, 2.4.).

Application No: 10/781,047
Docket No.: 57559/70207

Therefore, the Desiderio reference cannot be cited as a basis for an obviousness rejection of claims 6-22 and 25 in the present application. Applicants respectfully request reconsideration.

In view thereof, reconsideration and withdrawal of the §103 rejections are requested.

Applicant submits that all claims are allowable as written and respectfully request early favorable action by the Examiner. Applicant's representative would like to discuss this case with the Examiner to learn if any outstanding issues remain after consideration of this Amendment. If the Examiner believes that a telephone conversation with Applicants' attorney would expedite prosecution of this application, the Examiner is cordially invited to call the undersigned attorney of record. The Applicants believe that a one-month extension of time is required.

In view of the above amendment, applicant believes the pending application is in condition for allowance.

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Respectfully submitted,

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From the teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

Applicants respectfully disagree. The cited reference discloses the use of two, differently labeled peptide internal standards (page 5, 2.4 of Desiderio). All of the currently pending claims, as amended, require only one labeled peptide internal standard. The Desiderio reference cannot be cited as a basis for an obviousness rejection of claims 6-22 and 25 in the present application.

It is well-known that to establish a *prima facie* case of obviousness, three basic criteria must be met: (1) there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings; (2) there must be a reasonable expectation of success; and (3) the prior art reference(s) must teach or suggest all the claim limitations. The teaching or suggestion to make the claimed combination and the reasonable expectation of success must both be found in the prior art, and not based on applicant's disclosure. *In re Vaeck*, 947 F.2d 488, 20 USPQ2d 1438 (Fed. Cir. 1991). See MPEP § 2143.

There is no suggestion or motivation in the reference or in the knowledge generally available to one of ordinary skill in the art, to modify the cited reference to make the claimed invention, nor is there a reasonable expectation of success.

Furthermore, there was long felt need for the use of a single labeled peptide internal standard. A period of five (5) years passed between the publication date of the Desiderio reference and the filing date of the present application.